UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ENZO BIOCHEM, INC. et al.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	03 CV 3816 (RJS)
	)	
MOLECULAR PROBES, INC.,	)	
	)	
Defendant,	)	
and	)	**ORAL ARGUMENT REQUESTED**
	)	
YALE UNIVERSITY,	)	
	)	
Nominal Defendant.	)	

DEFENDANT MOLECULAR PROBES, INC.'S RESPONSE TO ENZO'S RULE 56.1 STATEMENT OF MATERIAL FACTS IN SUPPORT OF ENZO'S OPPOSITION TO MPI'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NON-INFRINGEMENT, AND IN SUPPORT OF ENZO'S CROSS-MOTION ON CLAIM CONSTRUCTION AND PARTIAL SUMMARY JUDGMENT OF VALIDITY

Pursuant to Local Rule 56.1 of the Local Rules of the United States District Court for the Southern District of New York, Defendant Molecular Probes, Inc. ("MPI") sets forth the following responsive statements to Plaintiffs Enzo Biochem, Inc.'s and Enzo Life Sciences, Inc's (collectively, "Enzo") Response to MPI's Rule 56.1 Statement of Material Facts in Support of MPI's Motion for Partial Summary Judgment of Non-Infringement and Enzo's Rule 56.1 Statement of Material Facts in Support of its Cross-Motion on Claim Construction and Partial Summary Judgment of Validity. In support, MPI states as follows:

MPI's Responses to Enzo's Statement Of Material Facts In Support Of Its Cross-Motion

Enzo No. 1:

Enzo accused MPI's ULYSIS products of infringing claims 1-3 ("the Claims") of the U.S. Patent No. 5,241,060 ("the '060 patent"). (Ex. 1 (5/17/05 Enzo Infringement Contentions); Declaration of Eric M. Jaegers's[sic] in Support of MPI's Motion ("Jaegers Decl."), Ex. 4 at 42.)

MPI Response to Enzo No. 1:

Disputed. Enzo accuses the ULYSIS products of infringement under claim 1 only. *See, e.g.*, MPI Exhibits 2 and 8. To the extent Enzo ever accused the ULYSIS products under claims 2 and/or 3, Enzo has waived or abandoned such claims through subsequent infringement contentions (*e.g.* Sept. 22, 2006), submissions and representations to the Court in its May 15, 2007 and December 13, 2011 responses (including exhibits) in opposition to the Defendants' joint motions for summary judgment on patent claims, and through other admissions or omissions. Those subsequent infringement contentions, court filings and admissions/omissions establish Enzo's current infringement contentions, which do not accuse the ULYSIS products under claim 2 or 3.

Enzo No. 2:

Enzo accused MPI's ChromaTide products of infringing the Claims of the '060 patent. (Ex. 1.)

MPI Response to Enzo No. 2:

Disputed and irrelevant. MPI has many ChromaTide products, and it is unknown which "ChromaTide products" Enzo is referring to. Undisputed that Enzo currently accuses four ChromaTide products of infringing claims 1 and 2 only (ChromaTide Alexa Fluor 488-7-OBEA-dCTP (C-21555), ChromaTide Alexa Fluor 546-16-OBEA-dCTP (C-21556), ChromaTide Alexa Fluor 594-7-OBEA-dCTP (C-21558), and ChromaTide Alexa Fluor 647-12-OBEA-dCTP (C-21559)). *See, e.g.*, MPI Exhibits 2 and 8; *see also* Enzo's subsequent infringement contentions and Enzo's May 15, 2007 and December 13, 2011 responses (and exhibits) in opposition to

Defendants' joint motion for summary judgment on patent claims. MPI disputes that any other ChromaTide products are accused under any claims or patents. Enzo No. 2 also is irrelevant because no ChromaTide products are involved in MPI's current motion for summary judgment and therefore any issues involving these products are not before the Court. The Court has authorized briefing and argument only on the issue of non-infringement of the ULYSIS products (Dkt. No. 116), and it further stated that it "will not consider and Defendants need not brief Plaintiffs' cross-motion; instead, Defendants should confine their reply to Plaintiffs' statements to the PTO and the effect of those statements on Plaintiffs' infringement claims." *See* Dkt. No. 130.

Enzo No. 3:

Claim 1 of the '060 patent claims:

> A nucleotide having the formula PM-SM-BASE-Sig wherein PM is a phosphate moiety, SM is a sugar moiety, BASE is a pyrimidine, purine or 7-deazapurine moiety, PM being attached at the 3' or the 5' position of SM when the nucleotide is a deoxyribonucleotide and at the 2', 3' or 5' position when the nucleotide is a ribonucleotide, BASE being attached to the 1' position of the SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or a 7-deazapurine, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine, at a position other than the C8 position when BASE is a purine and at a position other than the C7 position when BASE is a 7-deazapurine and wherein Sig represents a detectable moiety.

(Ex. 2 ('060 patent) at col. 31, lines 14-28.)

MPI Response to Enzo No. 3:

Undisputed that Enzo No. 3 correctly recites claim 1.

Enzo No. 4:

Claim 2 of the '060 patent claims:

> An oligo- or polydeoxyribonucleotide comprising at least one nucleotide in accordance with claim 1.

(Ex. 2 at col. 31, lines 29-30.)

MPI Response to Enzo No. 4:

Undisputed that Enzo No. 4 correctly recites claim 2. Irrelevant because Enzo does not accuse the ULYSIS products under claim 2 (*see, e.g.*, MPI Exhibits 2 and 8), and because issues relating to claim 2 are not before the Court. The Court has authorized briefing and argument only on the issue of non-infringement of the ULYSIS products (Dkt. No. 116), and it further stated that it "will not consider and Defendants need not brief Plaintiffs' cross-motion; instead, Defendants should confine their reply to Plaintiffs' statements to the PTO and the effect of those statements on Plaintiffs' infringement claims." *See* Dkt. No. 130.

Enzo No. 5:

Claim 3 of the '060 patent claims:

> An oligo- or polyribonucleotide comprising at least one nucleotide in accordance with claim 1.

(Ex. 2 at col. 31, lines 3 1-32.)

MPI Response to Enzo No. 5:

Undisputed that Enzo No. 5 correctly recites claim 3. Irrelevant because Enzo does not accuse the ULYSIS products under claim 3 (*see, e.g.*, MPI Exhibits 2 and 8), and because issues relating to claim 3 are not before the Court. *See also* MPI's Response to Enzo No. 4.

Enzo No. 6:

Hybridization of nucleic acids (i.e., oligo- or polynucleotides such as DNA, RNA, etc) is a process that involves the formation of a double-stranded DNA, RNA, or RNA-DNA hybrid from two individual complementary oligo- or polynucleotides. (Ex. 14 (5/15/07 Sinden Decl.) ¶ 26.)

MPI Response to Enzo No. 6:

Disputed and irrelevant. Disputed at least in part because oligo- and polynucleotides may self-hybridize. Issues of hybridization (or construction thereof) are not relevant to MPI's current

motion for summary judgment and therefore are not before the Court. Construction of any terms is not necessary. *See* MPI's Reply Brief. The Court has authorized briefing and argument only on the issue of non-infringement of the ULYSIS products (Dkt. No. 116), and it further stated that it "will not consider and Defendants need not brief Plaintiffs' cross-motion; instead, Defendants should confine their reply to Plaintiffs' statements to the PTO and the effect of those statements on Plaintiffs' infringement claims." *See* Dkt. No. 130.

Enzo No. 7:

To detect a target nucleic acid, one adds a hybridization probe (a short piece of DNA or RNA labeled as described in the '060 patent) to a sample of nucleic acids and then the probe hybridizes with a target DNA sequence. (*Id* ¶¶ 27-28.)

MPI Response to Enzo No. 7:

Disputed and irrelevant. Issues of hybridization (or construction thereof) are not relevant to MPI's current motion for summary judgment and therefore are not before the Court. Construction of any terms is not necessary. *See* MPI's Reply Brief. The Court has authorized briefing and argument only on the issue of non-infringement of the ULYSIS products (Dkt. No. 116), and it further stated that it "will not consider and Defendants need not brief Plaintiffs' cross-motion; instead, Defendants should confine their reply to Plaintiffs' statements to the PTO and the effect of those statements on Plaintiffs' infringement claims." *See* Dkt. No. 130

Enzo No. 8:

The '060 patent specification creates a special definition for the term "nucleotide":

> In accordance with the practices of this invention nucleotides are modified, such as at the 5 position of pyrimidine or the 7 position of purine, preparatory for the preparation therefrom of nucleotide probes suitable for attachment to or incorporation into DNA or other nucleic acid material. In the practices of this invention nucleotides, i.e. nucleic acids, preferably are modified in a non-disruptive manner such that the resulting modified nucleotides are capable of incorporation into nucleic acids and once incorporated in nucleic acids the modified nucleotides do not significantly interfere with the formation or

> stabilization of the double helix formed of the resulting nucleic acids containing the modified nucleotides. The non-disruptive modification of nucleotides and nucleic acids incorporating such modified nucleotides is in contrast with those modifications of nucleotides which are characterized as a disruptive modification in the sense that the resulting disruptively modified nucleotides and nucleic acids containing the same block proper double helix formation. In the practices of this invention, the nucleotides are desirably modified at the 5 position of the pyrimidine or the 7 position of the purine. The nucleotides so modified are non-disruptively modified and nucleic acids containing such nucleotides are capable of forming a double helix arrangement.

(Ex. 2 at col. 2, line 57 to col. 3, line 14; *see also* Ex. 18 (3/29/07 Keana Depo Tr.) at 72:14-75:7); Ex. 14 (5/15/07 Sinden Decl.) at ¶ 185; Ex. 12 (5/6/13 Enzo Response to PTO) at 8; Ex. 13 (5/6/13 Declaration of Dr. Rokita) ¶ 6.)

MPI Response to Enzo No. 8:

Undisputed that Enzo No. 8 correctly recites the referenced portion (Summary of the Invention) of the '060 patent. Disputed that Enzo's cited evidence supports that portion of the '060 patent, and further disputed that Enzo No. 8 is relevant. *See* MPI's Response to Enzo No. 6.

Enzo No. 9:

Enzo's Response and the Declaration of Dr. Rokita submitted therewith make reference to hybridization more than 40 times (26 mentions in Enzo's Response; and 16 in the supporting Rokita Declaration) in distinguishing MPI's prior art. (Ex. 12 and 13.)

MPI Response to Enzo No. 9:

Undisputed that Dr. Rokita's declaration and Enzo's Response reflect Enzo's opinions. Disputed that such opinions are correct or that Enzo No. 9 is relevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 10:

The '060 patent as originally filed specifically stated that the "modified polynucleotides" are used in "hybridization probes," including "gene mapping *in Situ* hybridization" and provided

a "General Protocol For Probe Detection Via *In Situ*, Colony, or Northern / Southern Hybridization Methods." (Ex. 17 ('060 patent file history) at 27-29.)

MPI Response to Enzo No. 10:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. Claim 1 does not include the words "modified polynucleotides." *See* MPI's Response to Enzo No. 6.

Enzo No. 11:

MPI asserts that the Claims of the '060 patent are invalid under 35 U.S.C. § 102 as follows: Draper et al., entitled "A Method for Linking Fluorescent Labels to Polynucleotides: Application to Studies of Ribosome-Ribonucleic Acid Interactions," Biochemistry 19(9): 1774-178 1, 1980 (hereinafter "Draper") anticipates claims 1 and 3 of the '060 patent; Eshaghpour et al., "Specific Chemical Labeling of DNA Fragments," *Nucleic Acid Research*, 7(6): 1485-1495, 1979 (hereinafter "Eshaghpour") anticipates claims 1 and 2 of the '060 patent; and Faust et al., "Synthesis of a Protein-Reactive ATP Analog and Its Applications for the Affinity Labeling of Rabbit-Muscle Actin," *Eur. J. Biochem*., 43:273-279, 1974 (hereinafter "Faust") anticipates claim 1 of the '060 patent. (Ex. 3 (1/3/07 Defendants' Joint Motion for Summary Judgment on patent issues) at 32; Ex. 4 (Draper (1980); Ex. 5 (Eshaghpour (1979); Ex. 6 (Faust (1974).)

MPI Response to Enzo No. 11:

Undisputed that MPI contends the '060 patent is invalid. Irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 12:

In connection with prior briefing on MPI's motion for summary judgment of invalidity of the '060 patent, Enzo stated, *inter alia*, that the construction and scope of the Claims of the '060 patent was as follows:

> In the context of the '060 patent, the Court acknowledged that Defendants failed to offer any testimony regarding the terms used in that patent. (Claim Construction Order, at 14). Nevertheless the Court correctly noted that the '060 patent describes "special nucleotides." (*Id.*) The specification of the '060 patent makes clear from the outset that the special nucleotides required by claim 1 must be useful for making probes and must be labeled in a non-disruptive manner "such that the resulting modified nucleotides are capable of incorporation into nucleic acids and once incorporated in nucleic acids the modified nucleotides do not significantly interfere with the formation or stabilization of the double helix formed of the resulting nucleic acids containing the modified nucleotides." (Ex. 58 ['060 patent] at col. 2, line 56 to col. 3, line 2 (emphasis added); *see also* Ex. 58 at col. 25, lines 11-16; col. 24, lines 17-23; Sinden Decl. ¶¶ 81-86.) Importantly, Defendants' witness on the '060 patent, Dr. Keana, agrees that the word "nucleotides" used in the context of the '060 patent refers to a nucleotide that is capable of incorporation into nucleic acids and that does not significantly interfere with the formation of the DNA double helix. (Keana Tr. 74:17, 75:7- 93:12, 93:17, Mar. 29, 2007 (Ex. 43).)
>
> As proven below, none of the nucleotides disclosed in Draper, Eshaghpour or Faust meet the requirements of the nucleotides claimed in the '060 patent. Specifically, the nucleotides disclosed in these references are unable to be incorporated into a polynucleotide and are not useful as a probe.

(Ex. 7 (5/15/07 Enzo Opposition to Defendants' Joint Motion for Summary Judgment on patent issues) at 35.)

MPI Response to Enzo No. 12:

Undisputed that Enzo No. 12 reflects Enzo's opinions. Disputed as untrue. Enzo No. 12 also is irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 13:

The '060 patent specification supports Enzo's construction. (*See e.g.*, Ex. 2 at col. 2, line 56 to col. 3, line 14; col. 24, lines 17-23; col. 25, lines 11-48.)

MPI Response to Enzo No. 13:

Disputed as untrue, and disputed that Enzo has proposed construction of any particular term. *See* MPI Exhibit 3. Further disputed in that no construction of any term is necessary. *See* MPI's Reply Brief. Enzo No. 13 also is irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 14:

In connection with briefing on MPI's prior motion for summary judgment of invalidity of the '060 patent, MPI disputed Enzo's proposed construction of the Claims. (Ex. 8 at 21, "However, as an initial matter, Enzo's arguments are based entirely on an improper reading of functional limitations into '060 claim 1 – i.e., that the claim 1 nucleotide is required to be 'incorporated into a polynucleotide' and to be 'useful as a probe.' *See* Opp. at 35. Enzo also reads in a limitation that a labeled mononucleotide must be 'enzymatically incorporated' into a polynucleotide. Opp. at 37. Enzo is wrong on both counts.")

MPI Response to Enzo No. 14:

Disputed that Enzo's construction of claim 1 is correct or that it has identified a term for construction. *See* MPI Exhibit 3. Also disputed that claim construction is necessary. *See* MPI's Reply Brief. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 15:

After Judge Sprizzo indicated that he was unlikely to grant MPI's motion for summary judgment of invalidity, MPI formally withdrew it. (Ex. 9 (7/17/07 H'rg Tr.) at 87:4-88:10.)

MPI Response to Enzo No. 15:

Disputed as stated and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 16:

Enzo's May 6, 2013 response ("Response") to a February 6, 2013 Non-Final Office Action issued by the PTO argued, *inter alia*, that the Claims should be construed such that the labeled mononucleotides of the Claims of the '060 patent must exist independently prior to their incorporation into an oligo- or polynucleotide hybridization probe:

IV. THE '060 PATENT

Generally, the '060 Patent relates to hybridizations probes. (*See* col. 2, lines 57- 62: "In accordance with the practices of this invention nucleotides are modified . . . *preparatory for the preparation therefrom of nucleotide probes* suitable for attachment to or incorporation into DNA or other nucleic acid material" (emphasis added)) and col. 25, lines 11-16: "A particularly important and useful aspect of the special nucleotides of this invention is the use of such nucleotides in the preparation of DNA or RNA probes. Such probes would contain a nucleotide sequence substantially matching the DNA or RNA sequence of genetic material to be located and/or identified."). The application as originally filed specifically stated that the "modified polynucleotides" are used in "hybridization probes," including "gene mapping *in Situ* hybridization" and further provides a "General Protocol For Probe Detection Via *In Situ*, Colony, or Northern / Southern Hybridization Methods." (pp. 27-29). Based on the above, Dr. Rokita explains that one skilled in the art would understand that the oligo- and polynucleotide probes of the '060 Patent claims must be capable of use as hybridization probes. (*See* Rokita Decl. ¶ 8).

More particularly, the patent relates to hybridization probes that are formed by first labeling a mononucleotide with a detectable moiety (termed "Sig" in the patent), and *subsequently* incorporating the labeled mononucleotide into an oligo- or polynucleotide probe using a polymerase (e.g., a terminal transferase). (*See* col. 2, lines 57-62; col. 25, lines 41-48).

Claim 1 of the '060 Patent recites "[a] nucleotide" defined by the formula "PM-SM-BASE-Sig" and Claims 2 and 3 each recite oligo- and polynucleotides "comprising at least one nucleotide in accordance with claim 1." The '060 Patent and its prosecution history make clear that claim 1 is directed to mononucleotides (as opposed to single nucleotide residues within oligo- or polynucleotides) and claims 2 and 3 are DNA or RNA probes into which a mononucleotide of claim 1 has been incorporated. (*See* Rokita Decl. ¶ 3). That means that the labeled mononucleotides of claim 1 must exist independently prior to their incorporation into the oligo- or polynucleotide probes of claims 2 and 3. (*Id.*). Dr. Rokita explains at length why one skilled in the art would understand that this is the only logical construction of the claims of the '060 Patent. (See Rokita Decl. ¶¶ 3-7).

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Further textual support for this construction is found in the '060 Patent's teaching that the claimed "PM-SM-BASE-Sig" compound is one of the "special nucleotides" in accordance with the invention (col. 22, lines 12-24 (emphasis added)) and that "[a] particularly important and useful aspect of the special nucleotides of this invention is the use of such nucleotides in the preparation of DNA or RNA probes" (col. 25, lines 11-13 (emphasis added)). (*See* Rokita Decl. ¶ 6).

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In fact, the '060 Patent requires that the labeled nucleotides "*are capable of incorporation* into nucleic acids and once incorporated in nucleic acids the modified nucleotides do not significantly interfere with the *formation or stabilization* of the double

> helix formed of the resulting nucleic acids containing the modified nucleotides." (col. 2, line 65-col. 3, line 2 (emphasis added)). Dr. Rokita explains that one skilled in the art understands that the claims of the '060 Patent require the nucleotide and label (i.e., "Sig") satisfy these conditions so that the resultant labeled nucleotide can be: (1) incorporated into a polynucleotide by a polymerase; and (2) used as a probe for PCR, Southern blots, Northern blots, *in situ* hybridization, sequencing, and chromosome mapping. (See Rokita Decl. ¶ 11).

(Ex. 12 at 6-9 (footnotes omitted).)

MPI Response to Enzo No. 16:

Undisputed that Enzo No. 16 reflects Enzo's opinion and that Enzo made such statements to the PTO. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Exhibit 3 and MPI's Response to Enzo No. 6.

Enzo No. 17:

On May 6, 2013, Enzo's expert Dr. Rokita stated his opinion that one skilled in the art would understand that the labeled mononucleotides of the Claims of the '060 patent must exist independently prior to their incorporation into an oligo- or polynucleotide hybridization probe:

> **I. Claim Construction**
>
> 3. Claim 1 of the '060 Patent refers to "[a] nucleotide" which is defined by the formula "PM-SM-BASE-Sig." Claims 2 and 3 each recite oligo- and polynucleotides "comprising at least one nucleotide in accordance with claim 1." Based on my review of the '060 Patent and its prosecution history, it is my opinion as one skilled in the art that claim 1 is directed to mononucleotides (as opposed to single nucleotide residues within oligo- or polynucleotides). It is further my opinion that claims 2 and 3 are DNA or RNA probes into which a mononucleotide of claim 1 has been incorporated. More specifically, any logical reading of these claims, consistent with the entire '060 Patent, requires that the labeled mononucleotides of claim 1 exist independently prior to their incorporation into the oligo- or polynucleotide probes of claims 2 and 3.
>
> ****
>
> .... It is also my opinion that claims 1-3 of the '060 Patent require that the labeled nucleotides be useful for making hybridization probes. This is supported by the Patent itself which teaches that "[a] particularly important and useful aspect of the special nucleotides of this invention is the use of such nucleotides in the preparation of DNA or RNA probes. Such probes would contain a nucleotide sequence substantially matching the DNA or RNA sequence of genetic material to be located and/or identified." (col. 25, lines 11-16) This is evident from the "Summary of the Invention" portion of the Patent

> which, as discussed above, states: "In accordance with the practices of this invention nucleotides are modified . . . preparatory for the preparation therefrom of nucleotide probes suitable for attachment to or incorporation into DNA or other nucleic acid material." (col. 2, lines 57-62 (emphasis added)) The application as originally filed specifically stated that the "modified polynucleotides" are capable of use as "hybridization probes," including "gene mapping *in Situ* hybridization" and provides a "General Protocol For Probe Detection Via *In Situ*, Colony, or Northern / Southern Hybridization Methods." ('060 Patent Application as filed, pp. 27-29) Based on the above, one skilled in the art would understand that the oligo- and polynucleotide probes of the '060 Patent claims must be capable of use as hybridization probes.

(Ex. 13 ¶¶ 1-6; *see also id.* ¶¶ 4-7, 11.)

MPI Response to Enzo No. 17:

Undisputed that Enzo No. 17 reflects Enzo's opinion and that Enzo's newest expert made such statements to the PTO. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Exhibit 3 and MPI's Response to Enzo No. 6.

Enzo No. 18:

Prior to filing its Motion for summary judgment of non-infringement, MPI rejected Enzo's July 17, 2013 Proposed Stipulation which proposed, *inter alia*, a dismissal of Enzo's infringement claim against the ULYSIS product. (Ex. 15 (July 2013 emails between parties) at 1)

MPI Response to Enzo No. 18:

Undisputed and irrelevant. *See* MPI's Response to Enzo No. 6.

Enzo No. 19:

Prior to filing its Motion for summary judgment of non-infringement, MPI rejected Enzo's July 17, 2013 Proposed Stipulation which proposed, *inter alia*, the following claim construction:

> The labeled mononucleotides of the Claims of the '060 patent must exist independently prior to their incorporation into an oligo- or polynucleotide hybridization probe.

(Ex. 15 (July 2013 emails between parties) at 1.)

MPI Response to Enzo No. 19:

Undisputed that Enzo proposed the construction and undisputed that Enzo does not identify a term for construction. Disputed that it is a correct or proper construction of any term of the '060 patent, or that any construction of any term is necessary. *See* MPI's Reply Brief and MPI's Exhibit 3. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 20:

Draper is a study of interactions between nucleic acids and ribosomes (proteins) that does not disclose hybridization probes. (Ex. 4; Ex. 12 at 9-13; Ex. 13 ¶¶ 10, 12-17; Ex. 14 ¶¶ 187-192; Ex. 18 at 132:10-133:8; 147:12-18.)

MPI Response to Enzo No. 20:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 21:

Draper is a study of interactions between nucleic acids and ribosomes (proteins) that does not first prepare a labeled mononucleotide and then incorporate the labeled mononucleotide into a probe, but rather reacts a polynucleotide with a label. (Ex. 12 at 9-10; Ex. 4 at pp. 1775-1776; Ex. 13 ¶¶ 10, 17; Ex. 14 ¶ 187.)

MPI Response to Enzo No. 21:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo Nos. 6 and 20.

Enzo No. 22:

The labeled NBF-CMP mononucleotide of Draper is not capable of incorporation into an oligo- or polynucleotide for use as a hybridization probe. (Ex. 4 at 1776; Ex. 14 at ¶ 189.)

MPI Response to Enzo No. 22:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 23:

The resulting Draper product destabilizes the ability of the polynucleotide to complex, i.e., hybridize, with complementary sequences. (Ex. 12 at 9-13; Ex. 13 ¶¶ 12-17; Ex. 14 ¶¶ 187-192; *see also* Ex. 18 at 132:10-133:8; 147:12-18; Ex. 1.)

MPI Response to Enzo No. 23:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 24:

The resulting Draper product creates polynucleotides with lowered stability. (Ex. 12 at 9-13; Ex. 13 ¶¶ 12-17; Ex. 14 ¶¶ 187-192; *see also* Ex. 18 at 132:10-133:8; 147:12-18; Ex. 1.)

MPI Response to Enzo No. 24:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 25:

The resulting Draper product uses chemistry that causes nucleotides within the polynucleotide to change which would interfere with base pairing. (Ex. 12 at 9-13; Ex. 13 ¶¶ 12-17; Ex. 14 ¶¶ 187-192; *see also* Ex. 18 at 132:10-133:8; 147:12-18; Ex. 1.)

MPI Response to Enzo No. 25:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 26:

The resulting Draper product leads to random labeling that is not useful for a hybridization probe. (Ex. 12 at 9-13; Ex. 13 ¶¶ 12-17; Ex. 14 ¶¶ 187-192; *see also* Ex. 18 at 132:10-133:8; 147:12-18; Ex. 1.)

MPI Response to Enzo No. 26:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 27:

The resulting Draper product uses a synthetic polynucleotide which has no naturally occurring complement it could hybridize and detect. (Ex. 12 at 9-13; Ex. 13 ¶¶ 12-17; Ex. 14 ¶¶ 187-192; *see also* Ex. 18 at 132:10-133:8; 147:12-18; Ex. 1.)

MPI Response to Enzo No. 27:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 28:

The resulting Draper product uses a label that may destabilize pairing with bases in a complementary nucleic acid. (Ex. 12 at 9-13; Ex. 13 ¶¶ 12-17; Ex. 14 ¶¶ 187-192; *see also* Ex. 18 at 132:10-133:8; 147:12-18; Ex. 1.)

MPI Response to Enzo No. 28:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 29:

The resulting Draper product uses a labeling method that is not suitable to label natural mRNA. (Ex. 12 at 9-13; Ex. 13 ¶¶ 12-17; Ex. 14 ¶¶ 187-192; *see also* Ex. 18 at 132:10-133:8; 147:12-18; Ex. 1.)

MPI Response to Enzo No. 29:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 30:

Draper does not anticipate the Claims of the '060 Patent under Enzo's proposed construction.

MPI Response to Enzo No. 30:

Disputed that Enzo has proposed a construction of a particular term of the '060 patent, and disputed that construction of any term of the patent is necessary. *See* MPI's Reply Brief. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 31:

Draper does not first prepare a mononucleotide and then incorporate the labeled mononucleotide into a probe as required by the claims of the '060 Patent. (Ex. 12 at 9-10; Ex. 14 at ¶¶ 187-189.)

MPI Response to Enzo No. 31:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 32:

Draper describes a method for attaching fluorescent labels to a nucleotide residue already within an intact synthetic polynucleotide called Poly(C). (Ex. 12 at 9-10; Ex. 4 at pp. 1775-1776; Ex. 13 ¶¶ 10, 17; Ex. 14 ¶ 187.)

MPI Response to Enzo No. 32:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 33:

Draper cannot anticipate the Claims of the '060 Patent under MPI's proposed construction.

MPI Response to Enzo No. 33:

Disputed that MPI offers a construction, and also disputed that construction is necessary. *See* MPI's Reply Brief. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 34:

Eshaghpour is a study of interactions between nucleic acids and proteins that does not disclose hybridization probes. (Ex. 12 at 14 (citing Ex. 5, Abstract); Ex. 13 at ¶ 19; Ex. 14 at ¶ 195; Ex. 18 at 142:19-143:6, 146:7-147:18.)

MPI Response to Enzo No. 34:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 35:

Eshaghpour does not first prepare a labeled mononucleotide and then incorporate the labeled mononucleotide into a probe. (Ex. 12 at 15 (citing Ex. 5 at Fig. 1, p. 1489); *see also* Ex. 13 at ¶ 20; Ex. 14 ¶ 194.)

MPI Response to Enzo No. 35:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 36:

Eshaghpour does not anticipate the Claims under Enzo's proposed construction.

MPI Response to Enzo No. 36:

Disputed that Enzo has proposed a construction of a particular term of the '060 patent, and disputed that construction of any term of the patent is necessary. *See* MPI's Reply Brief.

Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 37:

Eshaghpour adds a detectable label directly to an intact DNA polymer. (Ex. 12 at 15 (citing Ex. 5 at Fig. 1, p. 1489); *see also* Ex. 13 at ¶ 20; Ex. 14 ¶ 194.)

MPI Response to Enzo No. 37:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 38:

Eshaghpour does not add a labeled mononucleotide to an oligo- or polynucleotide. (*Id.*)

MPI Response to Enzo No. 38:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 39:

Eshaghpour first attaches a thiouridine nucleotide analog to the 3' end of a DNA strand and then links labels onto that nucleotide analog. (*Id.*)

MPI Response to Enzo No. 39:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 40:

Eshaghpour teaches the same mode of operation that MPI has represented to be employed by the ULYSIS products, i.e., to "label only oligo- or polynucleotides." (See MPI Motion at 9.)

MPI Response to Enzo No. 40:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 41:

Eshaghpour does not "label mononucleotides and then [] attach the labeled mononucleotides to a piece of DNA or RNA." (*See* MPI Undisputed Fact No. 25.)

MPI Response to Enzo No. 41:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 42:

Eshaghpour does not "first label[] a mononucleotide with a detectable moiety ..., and subsequently incorporat[e] the labeled mononucleotide into an oligo- or polynucleotide." (*See* MPI Undisputed Fact No. 23.)

MPI Response to Enzo No. 42:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 43:

Eshaghpour's labeled nucleotides do not "exist independently prior to their incorporation into [] oligo- or polynucleotide probes." (*See* MPI Undisputed Fact No. 24.)

MPI Response to Enzo No. 43:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 44:

Eshaghpour does not label mononucleotides. (*See* MPI Undisputed Fact No. 22.)

MPI Response to Enzo No. 44:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 45:

A prior art reference which labels oligo- and polynucleotides only cannot anticipate Claim 1 of the '060 patent. (*See* MPI Undisputed Fact No. 26.)

MPI Response to Enzo No. 45:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 46:

Eshaghpour cannot anticipate the Claims under MPI's proposed construction.

MPI Response to Enzo No. 46:

Disputed that MPI offers a construction, as no construction is necessary. *See* MPI's Reply Brief. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 47:

One skilled in the art would understand that the BASE moiety of the labeled mononucleotides of the Claims must be a purine, pyrimidine, or 7-deazapurine, and may not be a nucleobase analog other than 7-deazapurine. (Ex. 12 at 14-16; *see also* Ex. 13 ¶¶ 18-19; Ex. 2 at col. 20, line 59 to col. 21, line 43, col. 31, line 16.)

MPI Response to Enzo No. 47:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 48:

Enzo argued the following in the Response with respect to the understanding of a person of skill in the art that the BASE moiety of the labeled mononucleotides of the Claims must be a purine, pyrimidine, or 7-deazapurine, and may not be a nucleobase analog other than 7-deazapurine:

> Moreover, Claim 1 of the '060 Patent calls for a "pyrimidine, purine or 7-deazapurine." Dr. Rokita explains that the proper construction of the terms "purine" and "pyrimidine," as understood by one skilled in the art in view of the specification, includes the "major purines" and "minor purines" (identified at col. 20-2 1) and the "major pyrimidines" and "minor pyrimidines" (identified at col. 21), but does not include "*analogs*" of these nucleobases other than the specific 7-deazapurine analog explicitly mentioned in claim 1. (*See* Rokita Decl. ¶ 18). In fact, Dr. Rokita notes that the inclusion of 7-deazapurine in claim 1 would indicate to one skilled in the art that the claim does not include other "analogs" because, like 7-deazapurine, they would have been separately specified in the claims. (*Id.*)

(Ex. 12 at 14-16; *see also* Ex. 13 ¶¶ 18-19; Ex. 2 at col. 20, line 59 to col. 21, line 43, col. 31, line 16.)

MPI Response to Enzo No. 48:

Undisputed that Enzo No. 48 reflects Enzo's opinion. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Exhibit 3 and MPI's Response to Enzo No. 6.

Enzo No. 49:

Eshaghpour discloses a labeled 4-thiouridine analog. (Ex. 2 at col. 20, line 59 to col. 21, line 43, col. 31, line 16; Ex. 12 at 14-16; Ex. 13 ¶¶ 18-19; Ex. 14 ¶ 194; Ex. 18 at 140:2-142:2; Ex. 5 at pp. 1490.)

MPI Response to Enzo No. 49:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 50:

The labeled 4-thiouridine analog of Eshaghpour is not a purine, pyrimidine, or 7-deazapurine. (Ex. 2 at col. 20, line 59 to col. 21, line 43, col. 31, line 16; Ex. 12 at 14-16; Ex. 13 ¶¶ 18-19; Ex. 14 ¶ 194; Ex. 18 at 140:2-142:2; Ex. 5 at pp. 1490.)

MPI Response to Enzo No. 50:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 51:

Eshaghpour does not disclose a labeled purine, pyrimidine, or 7-deazapurine. (Ex. 2 at col. 20, line 59 to col. 21, line 43, col. 31, line 16; Ex. 12 at 14-16; Ex. 13 ¶¶ 18-19; Ex. 14 ¶ 194; Ex. 18 at 140:2-142:2; Ex. 5 at pp. 1490.)

MPI Response to Enzo No. 51:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 52:

The '060 Patent teaches that nucleotides of the invention containing the Sig component are equivalent to and useful for the same purpose as the nucleotides described in U.S. Patent No. 4,711,955 ("the '955 patent"). (Ex. 2 at col. 24, lines 58-64.)

MPI Response to Enzo No. 52:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Exhibit 3 and MPI's Response to Enzo No. 6.

Enzo No. 53:

The District Court has construed "nucleotide" in claim 1 in the related '955 Patent (incorporated by reference in the '060 patent) as being "comprised of otherwise naturally-occurring nucleotides which have been modified solely by the addition of at least one label . . . to a nitrogenous base . . . ." *Enzo Biochem, Inc. et al. v. Amersham PLC et al*., 439 F. Supp. 2d 309, 314 (S.D.N.Y 2006).

MPI Response to Enzo No. 53:

Disputed that the citation accurately reflects language in the Court's order relating to the term "nucleotide" as relevant in proper context, and disputed that construction of any terms is necessary here. *See* MPI's Reply Brief. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Exhibit 3 and MPI's Response to Enzo No. 6.

Enzo No. 54:

The inclusion of 4-thiouridine on a deoxyribose by Eshaghpour is not an "otherwise naturally-occurring nucleotide[]." (Ex. 12 at 16.)

MPI Response to Enzo No. 54:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 55:

The labeled 6-mercaptopurine analog of Eshaghpour is not a purine, pyrimidine, or 7-deazapurine. Ex. 12 at 17-18; Ex. 13 ¶ 21; Ex. 14 ¶ 197-198; Ex. 18 at 148:11-17; Ex. 3 at col. 20, line 59 to col. 21, line 43, col. 31, line 16.)

MPI Response to Enzo No. 55:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 56:

The inclusion of 6-mercaptopurine on a ribonucleotide would not be an "otherwise naturally-occurring nucleotide[]." (Ex. 12 at 18.)

MPI Response to Enzo No. 56:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 57:

Eshaghpour does not anticipate the Claims.

MPI Response to Enzo No. 57:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Exhibit 3 and MPI's Response to Enzo No. 6.

Enzo No. 58:

Faust is a study of nucleic acid interactions with proteins that does not disclose a labeled mononucleotide that is capable of incorporation into an oligo- or polynucleotide for use as a hybridization probe. (Ex. 12 at 16-17; Ex. 13 at ¶¶ 21-24; Ex. 14 ¶¶ 197, 199-200; Ex. 18 at 150:24-151:5.)

MPI Response to Enzo No. 58:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 59:

Faust does not anticipate Claim 1 under Enzo's construction.

MPI Response to Enzo No. 59:

Disputed that Enzo has proposed a construction of a particular term of the '060 patent, and disputed that construction of any term of the patent is necessary. *See* MPI's Reply Brief. Otherwise disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 60:

Faust does not disclose a labeled mononucleotide that is capable of incorporation into an oligo- or polynucleotide. (Ex. 12 at 16-17; Ex. 13 at ¶¶ 21-24; Ex. 14 ¶¶ 197, 199-200; Ex. 18 at 150:24-151:5.)

MPI Response to Enzo No. 60:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 61:

Faust has a label without a linker that would interfere with the base pairing necessary for incorporation into a nucleic acid. (Ex. 13 ¶¶ 21-24; Ex. 12 at 16-17; Ex. 14 ¶¶ 197-199.)

MPI Response to Enzo No. 61:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 62:

The specific purine analog disclosed by Faust is not covered by Claim 1. (Ex. 12 at 17-18; Ex. 13 ¶ 21; Ex. 14 ¶¶ 197-198; Ex. 18 at 148:11-17; Ex. 3 at col. 20, line 59 to col. 21, line 43, col. 31, line 16.)

MPI Response to Enzo No. 62:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 63:

The labeled analog of Faust is not a purine, pyrimidine, or 7-deazapurine. (Ex. 12 at 17-18; Ex. 13 ¶ 21; Ex. 14 ¶¶ 197-198; Ex. 18 at 148:11-17; Ex. 3 at col. 20, line 59 to col. 21, line 43, col. 31, line 16.)

MPI Response to Enzo No. 63:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 64:

The specific purine analog disclosed by Faust is not an analog of 7-deazapurine. (Ex. 12 at 17-18; Ex. 13 ¶ 21; Ex. 14 ¶¶ 197-198; Ex. 18 at 148:11-17; Ex. 3 at col. 20, line 59 to col. 21, line 43, col. 31, line 16.)

MPI Response to Enzo No. 64:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 65:

Faust does not disclose a labeled purine, pyrimidine, or 7-deazapurine. (Ex. 12 at 17-18; Ex. 13 ¶ 21; Ex. 14 ¶¶ 197-198; Ex. 18 at 148:11-17; Ex. 3 at col. 20, line 59 to col. 21, line 43, col. 31, line 16.)

MPI Response to Enzo No. 65:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 66:

The inclusion of the analog of Faust on a ribonucleotide would not be an "otherwise naturally-occurring nucleotide[]." (Ex. 12 at 18.)

MPI Response to Enzo No. 66:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Enzo No. 67:

Faust does not anticipate Claim 1.

MPI Response to Enzo No. 67:

Disputed and irrelevant to MPI's motion for partial summary judgment of non-infringement of the ULYSIS products. *See* MPI's Response to Enzo No. 6.

Respectfully submitted,

Dated: August 19, 2013

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that all counsel of record who have appeared and are deemed to have consented to electronic service are being served with a copy of the foregoing document (and all accompanying documents) via the Court's CM/ECF system per Local Civil Rule 5.2 on August 19, 2013. Any other counsel of record will be served with a true and correct copy of the foregoing by first-class mail or E-mail.

/s/ Eric M. Jaegers
Eric M. Jaegers